9. HARELIP (G1), HARELIP AND ASSOCIATED CLEFT PALATE (G2), AND POSTERIOR CLEFT PALATE (G3)

It has long been realized that many cases of harelip (G1) and harelip with cleft palate (G2) are similar in etiology. There have been numerous reports of monozygotic twins where both had G1 or G2 and of others where one twin had G1 and the other G2. Fogh-Andersen (1942), in his now classical report, was the first to point to the differing familial and epidemiological pattern of these conditions and that of posterior cleft palate (G3) with intact anterior palate and lip. There is an undue frequency of cases of G1 and G2 in some families and of G3 in others. However, cases of G1 or G2 and cases of cleft palate only (G3) do not occur in the same families more frequently than would be expected by chance. These findings have been confirmed in many studies, which may be exemplified by those of Fraser (1960), Fraser & Calnan (1961), Fujino et al. (1963) and Woolf et al. (1963). It is on such evidence and additional indications from the present data that cases of G1 and G2 are considered separately from those of G3 in what follows.

HARELIP (G1) AND HARELIP AND ASSOCIATED CLEFT PALATE (G2)

As mentioned above there is evidence from family and twin studies of the homogeneity of many cases of G1 and G2. This homogeneity is also evident on anatomical grounds. All degrees occur, from a slight " nick " in the lip to cases where the harelip is complete and there are in addition notches of varying depth in the alveolar margin. These defects represent essentially the end-results of different degrees of unsuccessful penetration of the mesoderm by those outgrowths from the ectodermal grooves which form the face. In these cases, the palatal lesion affects only the fusion of the palate or premaxilla which carries the incisor teeth. In cases where only harelip occurs in one member of the family and harelip and cleft palate in another the palatal cleft is almost invariably of this limited type (Kernahan & Stark, 1958). However, there are also cases of harelip and cleft palate where the palatal lesion is much larger, extending far back into the posterior palate in the midline, so that the cleft is complete or nearly complete.

Fusion of the face and the anterior palate is normally complete by about the end of the seventh week of embryonic life. However, midline fusion of the posterior palate does not start until the ninth week and then proceeds from front to back. Closure is not complete until about the twelfth week. If the anterior failure is very gross, it is understandable that proper fusion, at least anteriorly, of the posterior palate is virtually impossible.

Such gross failure of anterior fusion may result if it is impossible for the lateral maxillary processes to meet the premaxilla which is developed from the fronto-nasal process. In some cases this situation may be the result of complete failure of proper development or descent of the fronto-nasal process. In its extreme form this maldevelopment leads to disorganization of the face when the orbits are very close together or fused and there is anophthalmia or microphthalmia. Several of these cases are classified in the N group, and others, probably of this group, have been classified as M when from a description such as " absence of face " it did not seem justified to classify them in G2.

In other cases the fronto-nasal process descends but it is abnormal and projects anteriorly on a different plane from the rest of the developing face, so that again there is nothing with which the lateral maxillary processes can fuse. In these cases the philtrum is usually on the tip of the nose.

Both the above types of developmental failure appear almost invariably to determine also failure of fusion of the whole of the posterior palate. Developmentally, they are quite different in origin from simple cleft lip or such cleft with extension to the anterior palate only.

It will be clear from the above that we should expect some homogeneity in the etiology of G1 and G2 cases, as the minor degrees of G2 with an intact posterior palate are essentially greater degrees of G1. However, we should also expect some heterogeneity between G1 and G2 cases and within the G2 category because they would be expected to include also cases where grossly aberrant development of the fronto-nasal process was the primary defect.

HARELIP (G1) AND HARELIP AND CLEFT PALATE (G2) IN THE PRESENT DATA

Frequencies

From Table 9.1 it will be seen that in most centres there were more cases of G2 than of G1 and that, over-all, there were approximately twice as many cases of the former. There is a positive correlation between the frequencies of the two groups in the various centres (G1 and G2: $r = + 0.432$, $P < 0.05$).

Geographic and ethnic variations

The highest frequencies of G1 + G2 were in Johannesburg, Kuala Lumpur, Santiago, Hong Kong and Singapore. Direct comparisons have to be viewed with caution but these conditions are seldom missed at birth unless there is only a minimal notching of the lip. All the reported series used for examination of these influences appear to have been of cases presenting for surgical repair. On the basis of such data some authors have decided that birth order is the important variable (Fujino et al., 1963) and others that maternal age has the greater influence (Fraser & Calnan, 1961; Rank & Thomson, 1960). In the present data standardization for maternal age did not substantially influence relative frequencies and those in the centres mentioned above were still the highest.

Frequencies in ethnic groups

It has often been noted that frequencies were high in Asiatic people and in particular Japanese and Chinese (e.g., Neel & Schull, 1956). In Singapore the frequencies in Chinese, Malays and Indian ethnic groups were respectively 42/31 503 (1.33 per 1000), 10/4850 (2.06 per 1000) and 4/3085 (1.30 per 1000). In the same order in Kuala Lumpur the ethnic group frequencies were 15/8625 (1.74 per 1000), 5/2151 (2.32 per 1000) and 3/4094 (0.73 per 1000). These figures suggest that the frequencies in Malays were at least as high as in Chinese. It is noteworthy, however, that in Manila in those classified as " Malay " the frequency of G1 + G2 was 1.11 per 1000, or little above the mean in all centres of 0.98 per 1000. In both Singapore and Kuala Lumpur, however, the frequency in Indians was the lowest of the three—about the mean of that in all centres and similar to the figures from Bombay and Calcutta. There were no cases in Cape Town, where the " Cape Coloured " population has a substantial contribution from Malay blood.

G1 and G2 : sex proportions ($M/M+F$)

In both G1 and G2 there was an excess of males; the sex proportions in the summed data from the centres being 0.62 and 0.65 respectively. In the two combined the proportion was 0.64. There appears from Table 9.1 to be a fairly consistent distribution of this male excess, even allowing for sampling fluctuations of rather small numbers. The similarity in the sex proportions of G1 and G2 accord with a hypothesis of considerable homogeneity of some cases at least in these groups.

G1 and G2 : mortality

Of 407 infants with G1 or G2, 47 were stillborn or died in hospital, a mortality of 115 per 1000 total births. This is significantly higher than in all single births (16 617/416 615; $P < 0.001$). Some of the children who died may have had associated internal malformations which determined death. Unfortunately, only a few of these cases were examined at autopsy. It might be surmised that a proportion of children who died had a type of G1 or G2 which was the effect of homozygosity for a recessive gene. However, of the 47 who died three were the offspring of related parents. Seventeen of the surviving children had consanguineous parents. (Consanguinity associated with these and other malformations is considered in section 19.)

Harelip (G1) and harelip and cleft palate (G2) occurring as one of two or more malformations in the same child (Group N)

G1 and G2 occur frequently as one of several malformations (i.e., N group). One of these defects was found in 56 of 329 (17.0%) of those classified in the N group. Of these 56 infants, 30 (53.6%) were stillborn or died in hospital. This high mortality is partly, but probably not entirely, explicable in terms of the severity of associated malformations. The malformation groupings are shown in Table 9.2.

It seems likely, as already mentioned, that a few other cases are also closely related in etiology—namely, those said to have absence of the face, which probably means complete failure of development of the fronto-nasal process, so determining malformations not really differentiable from some of the cases called anophthalmia or microphthalmia with harelip and cleft palate.

A remarkable feature of multiple malformations which include G1 or G2 is the high proportion of males. In one of the 56 cases the sex was indeterminate but of the remaining 55, 43 were males, a pro-

portion (M/M+F) of 0.78. This is even higher than in cases where G1 or G2 was the only malformation.

There is an excess of males in all the N group, the sex proportion of all when the sex was distinguishable being 195/316, or 0.62. However, in those with and without G1 or G2 the proportions were respectively 43/55 and 152/261 ($\chi^2 = 6.89$; $P<0.01$) so that there is still a significant excess of males where G1 or G2 was one of the malformations, even within the multiple group.

Twinning and harelip (G1) and harelip and cleft palate (G2)

There is confirmation of the homogeneity of some cases of harelip (G1) and harelip and cleft palate (G2) in that in a pair of MM twins one had G1 and one G2. In another MM pair one had harelip (G1) and the other hyposapadias. In seven MM pairs one had G1 or G2 and the other was normal. In two FF pairs one was normal and the other had harelip and cleft palate (G2). In the only MF pair in the study where both infants had an abnormality, the male had harelip and cleft palate and the female had an interventricular septal defect. (This is a combination not infrequently seen in the *same* child; it was encountered in a pair of sibs referred to this Unit.)

CLEFT PALATE (G3)

Posterior cleft palate alone (G3) is inevitably midline and results from failure of fusion of the maxillary palatal processes determining failure of separation of the mouth from the nasal cavity. It may be complete up to the point of junction with the fronto-nasal process or incomplete anteriorly. In the least degree there may only be a cleft of the soft palate or even only a bifid uvula. There is a small increase in the frequency among close relatives of index cases relative to that in the population. A female excess has been described in most series.

Frequency of cleft palate as the only recorded defect in the present data

The summed frequency of G3 is about 0.23 per 1000 births, or rather less than a quarter of that of G1+G2. There is no suggestion of relatively high frequencies in Asian populations (Table 9.1).

Sex proportion (M/M+F)

Of 97 cases 40 were males, a proportion of 0.41, which is not significantly different at a 5% level from the sex proportion in all single births. The proportion is, however, significantly different from that found for G1 and G2 ($P<0.001$).

Mortality

Fifteen of the 97 affected infants were stillborn or died in hospital. This is significantly higher than the mortality in all single births (16 617/416 695; $P<0.001$). As in the case of the excess mortality in infants with G1 and G2, it is difficult to explain this finding in terms of the effects only of the anatomical defect and there is no association of the mortality with consanguinity of parents.

Cleft palate (G3) occurring as one of two or more malformations in the same child (i.e., in N group)

G3 also occurred in a number of cases in the N group and of 37 cases 18 were males. The mortality in these cases was high, 19 being stillborn or dying in hospital (9 males and 10 females). The malformations associated are shown in Table 9.3.

Twinning and cleft palate (G3)

Only one case of cleft palate alone occurred in twins. In one MF pair the male was affected and the female normal.

COMPARISON OF THE DATA ON HARELIP (G1), HARELIP AND CLEFT PALATE (G2) AND CLEFT PALATE (G3)

The higher frequency of G1+G2 than of G3 has already been noted, as has the significant positive correlation of the frequencies of G1 and G2.

There are, however, no such correlations of frequencies between G1 and G2 and that of G3:

G1 and G3	$r = -0.384$;	$P > 0.05$
G2 and G3	$r = -0.400$;	$P > 0.05$
G1 + G2 and G3	$r = -0.460$;	$P < 0.05$

Indeed, there is a suggestion of a negative correlation. This is an interesting indirect confirmation of the evidence from familial data of different etiology of G1 and G2 and of G3.

DISCUSSION

From the data there is confirmation of other evidence that isolated cleft palate (G3) is different from G1 and G2 in etiology. The relatively low correlation between the frequencies of G1 and G2 appears to support the other evidence reviewed that, although there is some homogeneity in origin of these cases, not all merely represent different degrees of the same developmental failure.

In addition to the reasons for heterogeneity advanced, it has to be remembered that there is at least one single dominant gene mutation which determines a syndrome of which G1 or G2 forms a part. The complete syndrome includes fistulae in the lower lips and syndactyly. However, the latter is by no means always present and the pits may be inconspicuous so that the condition may be commoner than usually realized and contribute more than supposed to familial incidence. It is possible that there are other such specific gene traits.

Most series of cases of G3 seen by surgeons include subjects which are examples of Pierre Robin syndrome and these cases, also due to dominant genes with somewhat irregular manifestation, no doubt contribute to the familial concentration of cases of G3. In the present report cases described as Pierre Robin syndrome are grouped as K4, and have not been discussed in this chapter. No doubt, however, examples of this syndrome have been included in G3 and N as well as in M.

It should be emphasized how high is the early mortality in infants with G1, G2 and G3, even when there are no other malformations. It follows that the cases seen by surgeons with a view to repair are a selected population of survivors.

TABLE 9.1

HARELIP, HARELIP AND CLEFT PALATE, AND CLEFT PALATE (NOT ASSOCIATED WITH OTHER MALFORMATIONS) (G1-G3) IN SINGLE BIRTHS

CENTRE		Harelip (G 1)				Harelip and Cleft palate (G 2)				G 1 + G 2				Cleft palate (G 3)			
		Number of cases			Per 1000 total births	Number of cases			Per 1000 total births	Number of cases			Per 1000 total births	Number of cases			Per 1000 total births
		M	F	T		M	F	T		M	F	T		M	F	T	
I 1	MELBOURNE	2	2	4	0.51	5	1	6	0.76	7	3	10	1.27	0	1	1	0.13
I 2	MELBOURNE	0	0	0	-	0	0	0	-	0	0	0	-	2	0	2	0.51
II	SAO PAULO	3	2	5	0.35	6	3	9	0.62	9	5	14	0.97	4	1	5	0.35
III	SANTIAGO	11	7	18	0.76	4	5	9	0.38	15	12	27	1.52	1	5	6	0.25
IV 1	BOGOTA	3	6	9	0.48	12	3	15	0.80	15	9	24	1.28	1	2	3	0.16
IV 2	MEDELLIN	12	1	13	0.64	11	3	14	0.68	23	4	27	1.32	0	0	0	-
V	CZECHOSLOVAKIA	4	1	5	0.25	6	1	7	0.35	10	2	12	0.60	3	7	10	0.50
VI	ALEXANDRIA	2	2	4	0.42	5	0	5	0.52	7	2	9	0.94	0	0	0	-
VII	HONG KONG	3	1	4	0.41	3	7	10	1.01	6	8	14	1.42	1	1	2	0.20
VIII 1	BOMBAY	9	5	14	0.35	16	13	29	0.73	25	18	43	1.09	2	3	5	0.13
VIII 2	CALCUTTA	3	3	6	0.31	3	3	6	0.31	6	6	12	0.62	3	0	3	0.16
IX 1	KUALA LUMPUR	2	3	5	0.31	14	6	20	1.25	16	9	25	1.57	0	0	0	-
IX 2	SINGAPORE	6	2	8	0.20	28	20	48	1.21	34	22	56	1.41	5	8	13	0.33
X 1	MEXICO CITY	2	1	3	0.12	12	5	17	0.69	14	6	20	0.81	1	2	3	0.12
X 2	MEXICO CITY	1	0	1	0.07	3	1	4	0.28	4	1	5	0.35	1	0	1	0.07
XI	BELFAST	8	2	10	0.36	9	5	14	0.50	17	7	24	0.85	4	9	13	0.46
XII	PANAMA CITY	4	0	4	0.25	5	2	7	0.44	9	2	11	0.69	0	0	0	-
XIII	MANILA	4	6	10	0.34	14	9	23	0.78	18	15	33	1.11	3	9	12	0.40
XIV 1	CAPE TOWN	0	0	0	-	0	0	0	-	0	0	0	-	0	1	1	0.33
XIV 2	JOHANNESBURG	4	4	8	0.72	6	4	10	0.90	10	8	18	1.61	0	1	1	0.09
XIV 3	PRETORIA	0	1	1	0.10	0	0	0	-	0	1	1	0.10	4	0	4	0.40
XV	MADRID	2	4	6	0.30	3	4	7	0.35	5	8	13	0.66	3	4	7	0.35
XVI 1	LJUBLJANA	0	0	0	-	5	0	5	0.56	5	0	5	0.56	2	1	3	0.34
XVI 2	ZAGREB	1	0	1	0.12	3	0	3	0.36	4	0	4	0.48	0	2	2	0.24
	TOTAL	86	53	139	0.33	173	95	268	0.64	259	148	407	0.98	40	57	97	0.23

TABLE 9.2

HARELIP (G1) AND HARELIP AND CLEFT PALATE (G2) ASSOCIATED WITH OTHER MALFORMATIONS (N) IN SINGLE BIRTHS

Centre	No. in N group	Sex and survival	Consan-guinity	Malformations
Hong Kong	N 7	M SB	None	HL (R); syndactyly of toes (B); IVSD; overriding aorta
Czechoslovakia	N 23	M LBA	None	HL; hypospadias
Bogotá	N 12	M LBA	None	HL (L); polydactyly (R) (NFS)
Santiago	N 7	M LBA	None	HL (B); microphthalmia (L); facial papillomata
Bombay	N 10	M LBD	None	HL (NFS); talipes (R) (NFS); deformities of all 4 extremities (NFS)
Bombay	N 9	M LBD	None	HL (B); talipes equinovarus (L); valgus (R)
Hong Kong	N 5	M SB	None	HL (NFS); malformed ear; hands clubbed; two fingers missing (R); clubfoot (R)
Mexico 1	N 35	F LBA	None	HL (R); CHD (?) (NFS)
Medellín	N 10	F LBA	None	HL (NFS); talus valgus (NFS)
Medellín	N 12	NR SB	FC	HL (NFS); ambiguous genitalia
Johannesburg	N 11	M SB	None	HL/CP (B); anophthalmia; rudimentary penis; defective sternum; polydactyly (NFS) of hands and feet
São Paulo	N 8	M LBD	None	HL/CP (severe); absent nose; anotia; anophthalmia
São Paulo	N 2	M LBD	None	HL/CP; anophthalmia; papillomata of face; rudimentary penis
Manila	N 6	M LBD	None	HL/CP (L); diaphragmatic hernia; rudimentary penis and scrotum
Bombay	N 6	M LBD	None	HL/CP (NFS); phocomelia (arms and legs); hypoplastic penis; no scrotum; no vaginal orifice
Panama	N 11	M LBA	None	HL/CP (B); agenesis of penis
Czechoslovakia	N 5	M LBD	None	HL/CP (B); microcephaly; microcystic kidneys; hydro-nephrosis
Bombay	N 4	M LBA	FC	HL/CP (NFS); imperforate anus
Czechoslovakia	N 24	M LBA	None	HL/CP; micrognathia; polydactyly of hands and feet
Panama	N 1	M LBA	None	HL/CP (B); polydactyly of hands (B) (NFS)
Medellín	N 9	M LBA	FC	HL/CP (B); polydactyly (ulnar) (R); cranium bifidum
Medellín	N 14	M LBA	None	HL/CP (unilateral); polydactyly (ulnar) (R)
Medellín	N 5	M LBA	None	HL/CP (B); polydactyly (ulnar) (R); rudimentary testes
Medellín	N 6	M SB	None	HL/CP (B); agenesis of abdominal wall; polydactyly of hands and feet (NFS); microcephaly
Manila	N 3	M LBD	None	HL/CP (R); hypertelorism; polydactyly (NFS) (R); lungs both unilobar; microtia (L)
Bombay	N 8	M LBD	CFC	HL/CP (NFS); polydactyly (ulnar) (R); talipes equino-varus (B)
Singapore	N 3	M LBD	None	HL/CP (NFS); polydactyly (NFS) (B)
Ljubljana	N 1	M LBD	None	HL/CP (NFS); polydactyly (NFS); talipes equinovarus (R)
Mexico 1	N 25	M SB	None	HL/CP (R); polydactyly (radial) (R)
Bombay	N 7	M LBA	None	HL/CP (NFS); absence of digits on hand (R) and foot (R)
Johannesburg	N 13	M LBA	None	HL/CP (B); apical dystrophy of 5th finger (L); anomalies of toes 2 & 3 (R)
Cape Town	N 3	M LBD	None	HL/CP; elongated index fingers

TABLE 9.2 (*concluded*)

Centre	No. in N group	Sex and survival	Consanguinity	Malformations
Zagreb	N 4	M LBA	None	HL/CP (B); syndactyly and reduction deformities (hands and feet); talipes equinovarus (R)
Panama	N 9	M LBA	None	HL/CP (B); talipes equinovarus (B)
Medellín	N 15	M LBA	None	HL/CP (NFS); talipes equinovarus (R)
Medellín	N 7	M LBA	None	HL/CP (NFS); talipes valgus (B)
Mexico 1	N 5	M LBA	None	HL/CP (R); talipes talus (L)
Santiago	N 6	M LBA	None	HL/CP; gross deformity of right ankle joint
Mexico 1	N 17	M LBA	None	HL/CP (B); agenesis of legs
Czechoslovakia	N 20	M SB	None	HL/CP; exomphalos; chondrodystrophy; IVSD
Belfast	N 17	M LBD	NR	HL/CP (NFS); CHD (NFS); skeletal anomalies (NFS)
Belfast	N 1	M LBD	NR	HL/CP (NFS); hiatus hernia
Johannesburg	N 15	M LBD	None	HL/CP (B); inguinal hernia (Richter type)
Kuala Lumpur	N 6	M LBD	None	HL/CP (L); exomphalos (severe)
Manila	N 2	M LBA	None	HL/CP (L); hypertelorism; low-set ears; neck webbing; inguinal hernia (R); umbilical hernia
Manila	N 7	M LBA	LFC	HL/CP (NFS); hypoplastic breasts; shield-like chest
Manila	N 1	F LBD	None	HL/CP (R); microtia; congenital cataract; horseshoe kidney
Melbourne 2	N 1	F LBD	None	HL/CP; absent premaxilla; absent corpus callosum and occipital lobes; IVSD (large); patent foramen ovale; right-sided aorta; exomphalos; bicornuate uterus
Bogotá	N 2	F LBD	None	HL/CP (R); microphthalmia (L); hypoplasia of mandible
Mexico 1	N 36	F LBD	None	HL/CP (NFS); absence of nasal bones; keel-shaped chest
Bombay	N 5	F LBA	None	HL/CP (NFS); short arms and polydactyly (NFS) of hands; short right leg; pre-auricular tubercles
Mexico 1	N 6	F LBA	None	HL/CP (B); syndactyly of fingers 3 & 4 (R)
Belfast	N 11	F LBA	NR	HL/CP (NFS); deformed ear (NFS)
Kuala Lumpur	N 4	F LBD	None	HL/CP (B); defect of parietal bone
Mexico 1	N 8	F LBD	None	HL/CP (B); abnormal ear; absent meatus (L); hypoplasia of tongue
Johannesburg	N 5	F LBD	None	HL/CP; fusion/reduction anomalies of all extremities

TABLE 9.3. CLEFT PALATE (G3) ASSOCIATED WITH OTHER MALFORMATIONS (N) IN SINGLE BIRTHS

Centre	No. in N group	Sex and survival	Consanguinity	Malformations
Panama	N 10	M LBD	None	CP; IVSD; patent ductus; hydronephrosis and hydroureters (B)
Melbourne 1	N 6	M LBD	None	CP (posterior small); persistent left superior vena cava; IVSD; abnormal thumb (L); abnormal coccyx
Czechoslovakia	N 4	M LBA	None	CP (soft); coloboma iridis (NFS); aortic stenosis
Belfast	N 3	M LBA	NR	Absent soft palate; CHD (NFS); micrognathia
Zagreb	N 2	M LBD	None	CP; arachnodactyly; CHD
Mexico 1	N 24	M LBD	None	CP; aplasia of oesophagus and trachea; polydactyly (R); abnormal ear (R)
Mexico 2	N 6	M LBA	None	CP; microcephalus; polydactyly of hand (R) (NFS); micrognathia
São Paulo	N 1	M LBA	None	CP; large head; polydactyly of hands and feet
Manila	N 4	M SB	None	CP (NFS); polydactyly (NFS)
Czechoslovakia	N 31	M LBD	None	CP (B); syndactyly; hypospadias
Mexico 2	N 2	M LBD	None	CP; polydactyly and syndactyly of feet
Melbourne 1	N 1	M LBD	None	CP; hypospadias; undescended testes; malformed femur, tibia and feet; 1st and 2nd fingers only on disorganized hands
Bombay	N 11	M LBA	FC	CP (NFS); talipes (NFS) (B)
Mexico 2	N 11	M LBA	LFC	CP; micrognathia; abnormal position of ear (R)
Johannesburg	N 8	M LBA	None	CP; abnormal kidney (L); " Potter's facies "; CHD
Melbourne 1	N 10	M SB	None	CP; two-lobed right lung; undescended testicle
Melbourne 1	N 7	M LBA	None	CP; tracheo-oesophageal fistula
Zagreb	N 1	M LBA	None	CP; webbed neck; hyperextensibility of joints
Czechoslovakia	N 17	F LBA	None	CP; arthrogryphosis multiplex; IVSD; micrognathia; pseudohermaphrodite; talipes equinovarus; polydactyly of hands
Medellín	N 3	F LBA	None	CP (NFS); CHD
Czechoslovakia	N 15	F LBD	None	CP; pes valgus; patent ductus
Mexico 2	N 9	F LBA	None	CP; coarctation of aorta
Medellín	N 2	F LBD	None	CP (NFS); CHD
Manila	N 8	F LBD	None	CP (NFS); brachycephaly; craniostenosis; anophthalmia (L); microphthalmia (R); low-set ears; webbed neck; polydactyly (L); CHD; anal fissure extending to vagina; long fingers and toes
Mexico 1	N 19	F LBD	None	Absence of palate; absence nasal bones; absence of patellae; genu recurvatum (B); CDH (NFS); CHD (?); short legs
Ljubljana	N 10	F LBD	None	CP (NFS); anal atresia; polydactyly (hands) (B) (NFS)
Manila	N 5	F LBA	None	CP (NFS); absence of toes (R)
Zagreb	N 5	F SB	None	CP; everted hands; talipes equinovarus (B); abnormal lobulation of lungs
Panama	N 7	F LBA	None	CP; talipes equinovarus (B)
Medellín	N 1	F LBD	None	CP; talipes valgus (NFS); microstomia; micromelia
Bogotá	N 9	F LBA	None	CP (NFS); malformation of finger 1 (B)
Belfast	N 13	F LBD	NR	CP; micrognathia; other skeletal malformations
Belfast	N 2	F LBA	NR	CP; Klippel-Feil syndrome
Singapore	N 4	F LBA	LFC	CP; atresia of auditory meatus (R)
Singapore	N 2	F LBA	None	CP; imperforate anus
Bogotá	N 11	F LBD	None	CP (NFS); agenesis of external auditory meatuses; agenesis of nostrils
Czechoslovakia	N 12	F LBD	None	CP; exomphalos; fissured tongue; arcuate uterus